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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/846,033	04/30/2001	Edward Rebar	019496-005820US	4301

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EXAMINER

SEHARASEYON, JEGATHEESAN

ART UNIT	PAPER NUMBER
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1647

DATE MAILED: 05/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/846,033	Applicant(s) REBAR ET AL.	
	Examiner Jegatheesan Seharaseyon	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 February 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 67-71,75,77 and 95-103 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 67-71,75,77 and 95-103 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>2/17/2004</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. This office action is in response to the amendment and response filed on 2/17/04.

Claims 67-71, 75, 77, and 95-103 are pending.

2. Applicant's updating the priority information is acknowledged.

3. Applicant has appended the claims with the SEQ ID Nos. However, the specification has not been amended to provide the appropriate SEQ ID Nos.

4. The text of those sections of Title 35, U. S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112, 2nd paragraph, is withdrawn

5. Applicants arguments and amendments have obviated the rejections.

Claim Rejections - 35 USC § 103, are maintained

6. The rejection of claims 67-71, 75 and 77 under 35 USC 103 (a) as being unpatentable over Ferrara et al. (1997) in view of Cox, III et al. (6, 534, 261) is maintained for the reasons set forth in the previous Office Action mailed on the 12th of November 2003 pages 4-6. Applicant's arguments filed on 2/17/04 have been fully considered but are deemed to be not persuasive. Although, Ferrara et al. discuss the administration of VEGF₁₆₅ for the regulation of angiogenesis, contrary to Applicants assertion, the reference also discusses extensively the modulation of VEGF in pathological conditions including angiogenesis (see pages: 14-19). Ferrara reference specifically discusses the modulation of VEGF gene by HIF-1 protein, which is a transcription regulator (see page: 7). Therefore, the Office took the position that the Ferrara reference teaches the modulation of VEGF gene in pathological conditions

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including angiogenesis and does not restrict its analysis to the administration of VEGF₁₆₅ for the regulation of angiogenesis in the Office Action mailed on the 12th of November 2003. Contrary to Applicants assertions, the Office relied on the Ferrara et al. reference to teach the modulation of VEGF gene, angiogenesis, and its role in the treatment of several pathological conditions (see pages 1 and 14-19). Cox III, et al. reference was cited for the delivery of zinc finger binding protein delivery and modulation of cellular genes including VEGF (see column 51 and 52). In addition, Cox III, et al. reference teaches the newly added claim limitation of topical application of zinc finger protein (column 35, lines 30-35) and expression of the zinc finger protein in a specific tissue (column 36, lines 57-60).

Applicant without providing any fact or evidence is also arguing that, "all isoforms of VEGF are induced via administration of a zinc finger protein, it was not known that the aggregate effect of their different functions would be the same as that of the single isoform VEGF₁₆₅". In addition, the specification does not provide any support for the assertion that; "other isoforms might compete with VEGF₁₆₅ for binding to receptor inhibiting the effect of VEGF₁₆₅". Contrary to Applicants assertion that in pages 98-100 of the specification, there is evidence to indicate that administering a zinc finger protein induces all isoforms of VEGF that is effective in stimulating angiogenesis and wound healing, the specification in figures 17-21 only demonstrate the expression of VEGF-A gene.

Furthermore, Applicant asserts that the Office has provided insufficient motivation to modify the teachings of Ferrara by replacing the administration of single

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isoform of VEGF protein with the zinc finger protein. This is a total mischaracterization of the Office's position. The Office in the previous Office Action mailed on the 12th of November 2003 indicated that one of ordinary skilled in the art would introduce a zinc finger binding protein to an animal to target VEGF gene to modulate VEGF gene expression and not to replace the administration VEGF isoform (see pages 5 and 6 of the Office Action) as applicant asserts. Secondly, the modification of Ferrara et al.'s teachings occur by using zinc finger protein a transcription regulatory factor protein instead of hypoxia-inducible factor 1 the transcription regulatory factor described by Ferrara et al. Further, one of ordinary skill in the art would have been motivated to modulate angiogenesis by regulating the expression of VEGF gene, by introducing zinc finger protein to target a site on VEGF gene to regulate the VEGF gene expression. It is also noted that regulating angiogenesis will enable one to treat diseases such as ischemia as described in Ferrara et al (see page: 6 of the Office Action). In addition to ischemia, regulating the angiogenesis also will affect proliferative retinopathies, tumors, arthritis etc (see Ferrara page: 1).

Finally, with respect to Applicants arguments that there is no reasonable expectation for success is based on the notion that the Office intended to use zinc finger protein instead of using VEGF₁₆₅ isoform. As discussed above, the substitution occurs instead, for hypoxia-inducible factor 1, the transcription regulatory factor used for the modulation of VEGF gene. Therefore, the modulation of VEGF gene expression by the introduction of zinc finger proteins will regulate the various isoforms. Thus, claims 67-

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71, 75 and 77 remain unpatentable over Ferrara et al. (1997) in view of Cox, III et al. (6, 534, 261).

7. The rejection of claims 95 and 96-103 (newly added) under 35 USC 103 (a) as being unpatentable over Ferrara et al. (1997) and Baird et al. (6, 479, 654) in view of Cox, III et al. (6, 534, 261) is maintained is maintained for the reasons set forth in the previous Office Action mailed on the 12th of November 2003 pages 6-7. Applicant's arguments filed on 2/17/04 have been fully considered but are deemed to be not persuasive. Applicant's arguments with respect to Ferrara and Cox, III et al. references have been addressed above in paragraph 6. The Office reiterates its position that Ferrara et al. and Cox, III et al. references were introduced to teach the modulation of VEGF gene and introduction of zinc finger protein replacing hypoxia-inducible factor 1 the transcription regulatory factor respectively. The Office in paragraph 6 above discussed the motivation and expectation of success presented by these two references. The Office did not suggest or contemplate the administration of VEGF protein for wound healing as suggested by the Applicant.

Further, in reference to the argument that there is insufficient motivation to combine the teachings of Bird et al. with Ferrara, Bird et al. teaches that that the up regulation of VEGF expression is essential for tissue repair, e-g: in wound healing. Since, the administration of zinc finger protein modulates the expression VEGF gene one of skilled in the art would be motivated to administer zinc finger protein with reasonable expectation of success to treat conditions such as wound healing. Thus,

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claims 95 and 96-103 remain unpatentable over Ferrara et al. (1997) and Baird et al. (6, 479, 654) in view of Cox, III et al. (6, 534, 261).

8. No claims are allowable.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Contact Information

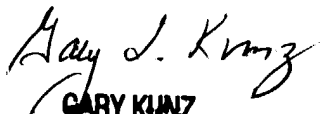
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon whose telephone number is 571-272-0892. The examiner can normally be reached on M-F: 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 571-272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JS 05/04


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